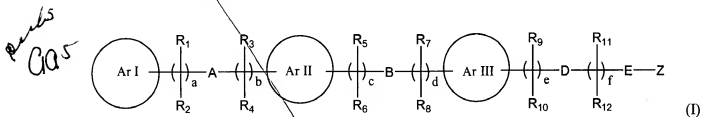


Abstract

This invention is directed to the use of triaryl acid derivatives of formula (I) and their pharmaceutical compositions as PPAR ligand receptor binders. The PPAR ligand receptor binders of this invention are useful as agonists or antagonists of the PPAR receptor.

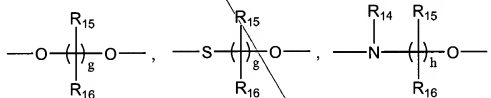


wherein:

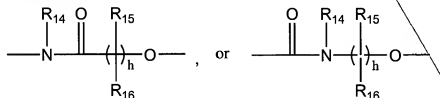


, and are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroaryl cycloalkenyl, fused heteroaryl cycloalkyl, fused heteroaryl heterocyclenyl, or fused heteroaryl heterocyclyl;

A is -O-, -S-, -SO-, -SO₂-, -NR₁₃-, -C(O)-, -N(R₁₄)C(O)-, -C(O)N(R₁₅)-, -N(R₁₄)C(O)N(R₁₅)-, -C(R₁₄)=N-,



a chemical bond.



B is $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-NR_{17}-$, a chemical bond, ethynylene, $-C(O)-$, $-N(R_{18})C(O)-$, or $-C(O)NR_{18}-$;

15 D is -O-, -S-, -NR₁₀-, a chemical bond, ethynylene, -C(O)-, -N(R₂₀)C(O)-, or -C(O)N(R₂₀)-;

E is a chemical bond or an ethylene group;

a is 0-4:

b is 0-4;

c is 0-4;

20 d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

his 1-4:

R_1, R_3, R_5, R_7, R_9 , and R_{11} , are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

$R_2, R_4, R_6, R_8, R_{10}$ and R_{12} , are independently $-(CH_2)_q-X$;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acylHNSO₂⁻, -

SR₂₃, Y¹Y²N- or Y³Y⁴NCO-;

Y¹ and Y² are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y¹ and Y² is hydrogen or alkyl and the other of Y¹ and Y² is acyl or aroyl;

Y³ and Y⁴ are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is R₂₁O₂C-, R₂₁OC-, cyclo-imide, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO-, R₂₁O- 2,4-thiazolidinedionyl, or tetrazolyl; and

R₁₉ and R₂₁ are independently hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R₁₃, R₁₇, R₁₉ and R₂₃ are independently R₂₂OC-, R₂₂NHOC-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R₁₄, R₁₅, R₁₆, R₁₈ and R₂₀ are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R₁₄ and R₁₅ taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R₁ radicals taken together with the carbon atoms to which the R₁ radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R₃ radicals taken together with the carbon atoms to which the R₃ radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R₅ radicals taken together with the carbon atoms to which the R₅ radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R₇ radicals taken together with the carbon atoms to which the R₇ radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R₉ radicals taken together with the carbon atoms to which the R₉ radicals are linked form an ethylene group; or

when f is 2-6; then vicinal R₁₁ radicals taken together with the carbon atoms to which the R₁₁ radicals are linked form an ethylene group; and

R₂₂ is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.